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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,491	05/31/2001	David H. Raulet	B01-088-1	8724

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EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,491	RAULET ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 19-38 have been added.

Claims 1-18 have been cancelled.

Claims 19-38 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

3. The disclosure is objected to because of the following informalities: on page 19, line 30 the recitation "250 mm2" is unclear. It is not clear if the "2" after the millimeters is a typographical error or to mean millimeters square.

Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 19-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants broadly claim a method for inhibiting metastatic prostate tumor growth comprising administering to the mammalian host a NKG2D-binding agent. Applicants are only in possession and the specification only provides support for a NKG2D-specific antibody and natural NKG2D ligands MICA, MICB and ULBP. The written description in this instant case only sets forth NKG2D-specific antibody and natural NKG2D ligands MICA, MICB and ULBP. Therefore the written description is not commensurate in scope with the claims drawn to any and all NKG2D-binding agents, which are multivalent and effective to inhibit growth of the tumor. Applicants are not in possession of any and all binding agents, which may or may not be effective in the manner germane to the claimed method.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence,

falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicant is only in possession of four species, a NKG2D-specific antibody and three natural ligands, MICA, MICB and ULBP. Applicants are not permitted to claim all agents encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. As Applicants' claims are written they encompass undefined binding agents, as well as binding ligands yet to be discovered. There is no information regarding the relation of structure to function of any other binding agents than the NKG2D-specific antibody and three natural ligands, MICA, MICB and ULBP. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph.

6. Claims 18-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants submit that "[t]he [new] claims have been restricted to targeting a particular type of tumor", see page 5 of Remarks. Applicants pointedly express that effective targeting of metastatic prostate tumor is specifically exemplified in Examples III and IV, page 18, line 17-page 25, line 9. Furthermore, Applicants aver, "the claims are limited to targeting a particular tumor type" and "...further functionally limited to those susceptible to the subject method". These remarks have been carefully considered but found unpersuasive.

The Examiner has reviewed the specification in particular pages 18 -21, Example III. The example reflects that cells from TRAMP-derived murine prostate cancer cell line, TRAMP-C2 (C2) have been transduced with NKG2D-ligands and administered to C57BL/6 male mice. The results provided in the bridging paragraphs of pages 20, 21 and 22, 23 support *in vivo* administration of NKG2D-ligand transduced cells can elicit an antitumoral response and reduce tumor incidence and severity of prostate lesions. The methodology listed in the specification is not commensurate in scope with claims.

It is art known that NKG2D ligands are expressed at high levels by tumor cells, see page 1, line 24 of the specification. It is clear that the native tumor cells used in the experimental methodology do not have the said ligands or these ligands are expressed in significantly low levels rendering these cells unable to mount an effective immunotherapeutic reaction. Tumor cells not transduced with NKG2D ligands would continue to present a problem to the host. Accordingly, the cancer would still be

prevalent with the potential to metastasize. Applicants' claims read on the administration of NKG2D-binding agents, but the experimental data provides the administration of transduced tumor cells with NKG2D ligand. There is no disclosure supporting administration of NKG2D ligands in isolation (without cells) or NKG2D-binding agents. Furthermore, scientific evidence supports these ligands are naturally present on tumor cells it seems that priming the cancer cells with additional ligands is the hallmark of the claimed invention. As the claims are presented the NKG2D-binding agents alone are to be administered. The claims do not provide language commensurate with the experimental data provided in the specification. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to practice the claimed method in a manner reasonably correlated with the scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 19-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 19 and 29 are vague and indefinite in the recitation "expressing native NKG2D". It is not clear how the host expresses the receptor. Are the tumor cells expressing the receptor? Due to the lack of clarity the metes and bounds of the claims cannot be determined.

b. The phrase "arising in situ" in claims 19 and 29 is vague and indefinite. It is not clear if this recitation is referring to one already determined to have metastatic prostate tumor or does one have the potential to have a tumor. Claims including the said phrase are unclear because it is unclear if the tumor has already metastasized, the tumor will be inhibited. The metes and bounds cannot be determined.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
March 24, 2003